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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	20

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/234,733	Jiang et al.
Examiner	**Art Unit**
Ja-Na Hines	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) X Responsive to communication(s) filed on *Jul 23, 2001*

2a) X This action is FINAL. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) X Claim(s) *1-12 and 44-55* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) X Claim(s) *1-12 and 44-55* is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are objected to by the Examiner.

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved.

12) The oath or declaration is objected to by the Examiner

Priority under 35 U.S.C. § 119

13) Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) All b) Some* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

DETAILED ACTION

Amendment Entry

1. The examiner acknowledges the amendment and declaration filed July 23, 2001. Claims 1-6 have been amended. Claims 44-55 have been newly added. Claims 1-12 and 44-55 are pending and under examination in this office action.

Specification

2. The use of the trademark TWEEN™ and other diagnostics and reagents have been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

3. The disclosure is objected to because of the following informalities: The new address of ATCC is 10801 University Boulevard, Manassas, VA 20110-2209. Appropriate correction is required.

The specification has not been checked to the extent necessary to determine the presence

which applicant may become aware in the specification.

Withdrawal of Rejections

4. In view of applicant's remarks and amendments to the claims, the following rejections are being withdrawn:

a) the rejection of claims 1-12 under 35 U.S.C. 101;

b) the rejection of claims 1-12 under 35 U.S.C. 102; and

c) the rejection of claims 1-12 under 35 U.S.C 103(a).

Maintained Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-12 and 44-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The isolated nucleic acid of the claims lacks any defining recites that the isolated nucleic acid molecule consist of a sequence encoding an immunogenic

polypeptide having at least 90% identity to amino acids 1-256 or 29-256 of SEQ ID NO:2. There is no structural criteria such as size or molecular weight, deposit information, or sequence information about the nucleic acid. Therefore, the identity of the nucleic acid is indefinite.

6. Claims 1-12 and 44-55 are rejected as being vague. The term "(SEQ ID NO:2)" in the claims is vague and indefinite. The metes and bounds of the claims cannot be determined as it is not clear as to whether the enclosed information is meant to be exemplary or limiting.

The claims refer to figures 4A-4C. However the claims should be self contained and not incorporate data from the drawings. Appropriate correction is requested.

7. Claims 1-12, 44, 46, 49, 52 and 55 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The new matter rejection is maintained. Applicants assert that support for the amended claims can be found on page 9, lines 17-20 and page 16 lines 16-21. The cited pages refer to proteins having amino acids sequences with substantially homologous sequence encoded by genes.

It is the examiner's position that there is no support for an immunogenic polypeptide

SEQ ID NO:2 is found. Nowhere in the specification or drawings is there data teaching an

isolated amino acid reciting the positions 29-256 with at least 90% sequence identity. Again, the claims incorporate new matter.

8. Claims 1-12 and 44-55 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid molecule comprising SEQ ID NO:1 which encodes the amino acid sequence of SEQ ID NO:2 does not reasonably provide enablement for an isolated nucleic acid molecule encoding a polypeptide having at least 90% sequence identity to amino acid positions 1-256 or 29-256. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims

The claims recite 90% sequence identity to SEQ ID NO:2 wherein the variant presumably can be obtained by deletion, substitution or insertion of one or more nucleic acids, however that specification provides no guidance as to what nucleic acids may or may not be changed without causing a detrimental effect to the polypeptide to be produced. The claim broadly teaches 90% sequence identity which includes substitution or insertion, therefore any amino acid is being claimed, and no specific location for where the deletion, substitution or insertion or any combination thereof is recited, if 10% of the nucleic acids are substituted or inserted the resulting encoded polypeptide could result in an polypeptide not taught and enabled

Furthermore, it is unclear how to define the nucleic acid molecule since the metes and bounds of the polypeptides are not known. Neither the claims nor the specification teach how to obtain a polypeptide by deletion, substitution or insertion of one or more nucleic acids. There is no guidance as to what nucleic acids may or may not be changed without causing a detrimental effect to the polypeptide being claimed. The claims broadly teach polypeptides which include substitution or insertion, therefore any polypeptide is being claimed, and no specific location for where the deletion, substitution or insertion or any combination thereof is recited. Thus, the resulting polypeptide could result in a polypeptide not taught and enabled by the specification.

Thomas E. Creighton, in his book "Protein structure: A Practical Approach, 1989; pages 184-186" teaches that present day site directed mutagenesis of a gene allows any amino acid in a protein sequence to be changed to any other, as well as introducing deletions and insertions. The reference goes on to teach that it is difficult to know which amino acid to change and which is the best residue to substitute for the desired functional and structural effect.

Nosoh, Y. et al in "Protein Stability and Stabilization through Protein Engineering, 1991" (chapter 7, page 197, second paragraph) adds support to Thomas E. Creighton, by teaching that results so far accumulated on the stability and stabilization of proteins appear to indicate that the strategy for stabilizing proteins differ from protein to protein and that any generalized mechanisms for protein stability have not yet been presented.

sequences; however, the specification provides no guidance as to what nucleotides may be

changed without causing a detrimental effect to the polypeptide to be produced. Further, it is unpredictable as to which nucleotides could be removed and which could be added. While it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where amino acid substitutions can be made with a reasonable expectation of success are limited. Other positions are critical to the protein's structure/function relationship, e.g., such as various positions or regions directly involved in binding, catalysis in providing the correct three-dimensional spacial orientation of binding and catalytic sites. These regions can tolerate only very little or no substitutions.

To start with the DNA sequence first, this requires even more work on the part of the skilled artisan. Applicants have provide no guidance to enable one of ordinary skill in the art how to determine, without undue experimentation, the effects of different nucleotide substitutions and the nature and extent of the changes that can be made. It is unclear that a polypeptide could be produced from the nucleotide segments drawn to less than the full-length protein. Selective point mutation to one key antigen residue could, in practical terms, eliminate the ability of an antibody to recognize this altered antigen. If the range of decreased binding ability after single point mutation of a protein antigen varies, one could expect point mutations in the protein antigen to cause varying degrees of loss of protection, depending on the relative importance to the binding interaction of the altered residue. Alternatively, the combined effects

protein having multiple antigenic sites, multiple point mutations, or accumulated point mutations

at key residues could create a new antigen that is precipitously or progressively unrecognizable by any of the antibodies in the polyclonal pool.

No working examples are shown containing the missing information. Without such information, one of skill in the art could not predict which deletions, substitutions or insertions or any combination thereof would result in the desired polypeptide. Accordingly, one of skill in the art would be required to perform undue experimentation to use any nucleic acid at any location to produce this polypeptide. Therefore, one skilled in the art could not make and/or use the invention without undue experimentation.

Response to Arguments

9. Applicant's arguments filed July 23, 2001 have been fully considered but they are not persuasive.

10. Applicants assert that they provide nucleic acid molecules that encode immunogenic polypeptides of SEQ ID NO:2 and the epitopes within need not be conformational. Applicants also submit that the one skilled in the art would not find it unduly burdensome to identify immunogenic polypeptides containing linear epitopes with 90% or more sequence identity to the amino acid sequence of SEQ ID NO:2. However, it is the examiner's position that applicants have not taught what 10% of the nucleic acids can be inserted, deleted or substituted to create

acid molecule with 90% sequence identity to SEQ ID NO:2. See also the associated rejection.

11. The declaration of Andrew A. Potter, Ph.D. under 37 CFR 1.132 filed July 23, 2001 is insufficient to overcome the rejection of claims 1-12 and 44-55 based upon insufficiency of disclosure under 35 USC 112, first paragraph as set forth in the Office action because: the Declaration does not teach that any an nucleic acid molecule capable of encoding the polypeptide with 10% of the nucleic acids substituted, deleted or added within which will lead to a predictable polypeptide. Neither the declaration nor the attached article state that undue experimentation will not be required for test every possible nucleic acid substitution. The declaration states opinions about non-prior art references, methods of gene isolation, protein purification and unexpected immunization results. The declaration states that a successful vaccine was developed, however that claims are not drawn to a mastitis vaccine but to an isolated nucleic acid molecule consisting of a sequence having at least 90% sequence identity to SEQ ID NO:2.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MEP. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is (703) 305-0487. The examiner can normally be reached on Monday through Thursday from 6:30am to 4:00pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Ja-Na Hines JH

October 2, 2001